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10/692,011	10/24/2003	Kenji Nakajima	Q78108	8536

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,011	NAKAJIMA, KENJI	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1,4,7,10 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-3, 5-6, 8-9, and 11-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 2-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Besemer et al (US 6,140,044).

In the instant claims, Besemer et al reference teaches an array of probes (i.e. bound ligands or bound receptors) on a wafer (i.e. biochemical analysis unit), wherein the wafer may contain depressed regions and surfaces on the wafer can be membranes (i.e. porous adsorptive regions), and wherein the wafer can be mounted in a 96-well microtiter format for parallel hybridization (i.e. plurality or regions). See column 5, line 41 to column 6, line 3; column 15, lines 57-67; and Figure 1a. In addition, Besemer et al teach the step of connecting the chip to a fluid delivery system that introduces fluids to contact the probes during the hybridization process (i.e. forcibly causing a receptor or ligand to flow across each of the porous adsorptive regions), wherein the fluid contains labeled targets (i.e. labeled receptor or labeled ligand; utilization of a labeling substance) that will hybridize with only complementary sequences on the substrate, and wherein reactions between the probes and targets are analyzed by imaging systems

(i.e. detecting the receptor or the ligand). See column 1, lines 24-40; column 12, lines 49-57; and column 13, lines 21-23. Furthermore, Besemer et al teach the step of removing bubbles (i.e. bubble removing and dissolving process) from the cavity by placing inlets and outlets at the highest and lowest positions in the cavity, respectively. See column 8, lines 13-15.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 8-9 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Besemer et al (US 6,140,044) in view of Bronstein et al (US 5,543,295).

Besemer et al reference has been disclosed above and additionally teaches that the targets (i.e. receptor or ligand) can be nucleic acids and can be labeled with an enzyme (i.e. auxiliary substance). See column 4, line 6; and column 3, lines 50-60.

However, Besemer et al fail to teach the step of forcibly causing a reaction liquid containing a labeling substance, which is capable of undergoing specific binding with the auxiliary substance, to flow such that the reaction liquid flows across each of the porous adsorptive regions of the biochemical analysis unit, the labeling substance, which is capable of undergoing specific binding with the auxiliary substance, thus being specifically bound to the auxiliary substance-bound receptor or the auxiliary substance-bound ligand having been specifically bound to at least one of the bound ligands, or to at least one of the bound receptors, and detecting the auxiliary substance-bound receptor or the auxiliary substance-bound ligand, which has been specifically bound to at least one of the bound ligands or at least one of the bound receptors, by the utilization of the labeling substance.

Bronstein et al teach the step of performing specific binding assays between two molecules and then exposing a dioxetane to the bound molecules, wherein an enzyme (i.e. auxiliary substance) tagged on one of the molecules cleaves an enzyme cleavable group on the dioxetane and causes a chromophore (i.e. labeling substance) bonded to the enzyme cleavable group to luminescence and be detected, in order to provide water soluble reporter molecules that can be used in bioassays. See column 17, line 66 to column 18, line 18; and column 2, lines 12-24. In addition, Bronstein et al teach that the enzyme can be bound to nucleic acid. See column 17, lines 62-63.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Besemer et al with the step of performing specific binding assays between two molecules and then exposing a dioxetane to the bound molecules, wherein an enzyme (i.e. auxiliary substance) tagged on one of the molecules cleaves an enzyme cleavable group on the dioxetane and causes a chromophore (i.e. labeling substance) bonded to the enzyme cleavable group to luminescence and be detected, as taught by Bronstein et al, in order to provide water soluble reporter that can be used in bioassays. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the steps of Bronstein et al, in the method of Besemer et al, since Besemer et al teach the specific binding of two molecules, wherein one molecule is labeled with an enzyme, and the steps of Bronstein et al produces bioassay detection through the cleavage of a labeling substance that is contacted with an enzyme labeled on one member of a specific binding pair.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 2-3, 5-6, 8-9, and 11-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/649,719 in view of Besemer et al (US 6,140,044).

The instant application recites an assay method using a biochemical analysis unit, comprising the steps of obtaining a biochemical analysis unit provided with a plurality of porous adsorptive regions, to which ligands or receptors have been bound respectively, and performing a specific binding detecting process comprising the steps of forcibly causing a receptor or a ligand to flow such that the receptor or the ligand flows across each of the porous adsorptive regions of the biochemical analysis unit, the receptor or the ligand being thus subjected to specific binding with the bound ligands or the bound receptors, the receptor or the ligand being thereby specifically bound to at least one of the bound ligands, or to at least one of the bound receptors, and detecting the receptor or the ligand, which has thus been specifically bound to at least one of the bound ligands or at least one of the bound receptors, by the utilization of a labeling substance, a liquid being forcibly caused to flow, such that the fluid flows across each of the porous adsorptive regions of the biochemical analysis unit, during the specific binding detecting process, wherein bubble removing processing for removing bubbles,

which are present in the liquid, from the liquid is performed during the flowing of the liquid.

The copending application teaches certain limitations of the instant application by reciting a chemical luminescence method using a biochemical analysis unit, comprising the steps of obtaining a biochemical analysis unit provided with a plurality of porous adsorptive regions, to which ligands or receptors have been bound respectively, subjecting a labeled receptor or a labeled ligand, which has been labeled with a labeling substance, to specific binding with the ligands or the receptor (i.e. specific binding detecting process) s, each of which has been bound to one of the porous adsorptive regions of the biochemical analysis unit, the labeled receptor or the labeled ligand thereby specifically bound to at least one of the ligands or at least one of the receptors, causing a chemical luminescence substrate to undergo a reaction with the enzyme-labeled antibody, which has been specifically bound to the labeled receptor or the labeled ligand (i.e. detecting the receptor or ligand; by utilization of a labeling substance), wherein, at the time at which the enzyme-labeled antibody is subjected to the specific binding with the labeled receptor or the labeled ligand, which has been specifically bound to at least one of the ligands or at least one of the receptors, a reaction liquid containing the enzyme-labeled antibody is forcibly caused to flow such that the reaction liquid containing the enzyme-labeled antibody flows across each of the porous adsorptive regions of the biochemical analysis unit (i.e. liquid being forcibly cause to flow during the specific binding process).

However, the copending application fails to teach the step wherein bubble removing processing for removing bubbles, which are present in the liquid, from the liquid is performed during the flowing of the liquid.

Besemer et al teach the step of removing bubbles from the cavity by placing inlets and outlets at the highest and lowest positions in the cavity, respectively, in order to improve fluid circulation. See column 8, lines 2-15.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of the copending application with the step of removing bubbles from the cavity by placing inlets and outlets at the highest and lowest positions in the cavity, respectively, as taught by Besemer et al, in order to improve fluid circulation. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of removing bubbles, as taught by Besemer et al, in the method of the copending application since both the copending application and Besemer et al are directed towards fluid flow on substrates for binding assays.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

8. Applicant's arguments, see pages 1-2 of the Remarks, filed 17 August 2005, with respect to the rejection of claims 2-3, 5-6, 8-9, and 11-12 under 35 U.S.C. 112, 2nd

paragraph have been fully considered and are persuasive. The rejection under 35 U.S.C. 112, 2nd paragraph of claims 2-3, 5-6, 8-9, and 11-12 has been withdrawn.

9. On pages 2-4 of the Remarks, Applicant traverses the rejection of claims 2-3 and 5-6 under 35 U.S.C. 102(b) as anticipated by Besemer et al (US 6,140,044). Applicant argues that (1) Besemer does not disclose, teach or suggest the porous adsorptive regions of the present invention, because the method steps to produce the probe array of Besemer and the adsorptive regions of the claimed invention are different, (2) Besemer allegedly does not teach the porous adsorptive regions since different bubbles are generated between Besemer and the claimed invention, and (3) Besemer does not teach or suggest causing fluid to flow across the porous adsorptive regions.

With regards to Applicant's first point above, Applicant specifically contends that the claimed invention forms holes by punching holes in a base plate and filling the holes with porous material, whereas Besemer teaches forming a probe array to synthesize different chemical compounds. See page 3, 1st paragraph.

Applicant's arguments have been fully considered but they are not persuasive. The specification does not define "porous adsorptive regions", but merely provides an example of what can constitute said regions. In addition, the instant claims are recited broadly enough to encompass embodiments other than the adsorptive regions that are disclosed in the specification. Claim 2 (line 7) and claim 5 (line 5) merely state "porous adsorptive regions of the biochemical analysis unit" and do not recite any other limitation that would suggest that the porous adsorptive regions are anything other than

regions that include porous, adsorptive material. Furthermore, Applicant cites column 4, lines 22-47 of Besemer as evidence that the probe array is different from the claimed adsorptive regions. However, Applicant is actually citing disclosure of the probe array itself, and not the surface that the array is immobilized upon. As stated in the previous Office Action and restated supra, the cited portion of Besemer in teaching the porous adsorptive regions is actually in column 6, line 2, which states that the surfaces on the wafer (i.e. biochemical analysis unit) can be membranes. One of ordinary skill in the art at the time of the invention would clearly recognize that membranes are porous, adsorptive materials. Therefore, since Besemer reference teaches porous, adsorptive membranes on the surface of a biochemical analysis unit, Applicant's arguments are not found to be convincing.

With regards to Applicant's second point above, on page 3, 2nd paragraph of the Remarks, Applicant specifically contends that "bubbles that cling to the adsorptive regions from in the present invention" whereas "bubbles are formed as a result of the use of nitrogen to introduce and circulate the fluid in Besemer".

Applicant's arguments have been fully considered but are not considered persuasive. Applicant does not present a convincing argument since the traverse merely states that the claimed invention forms bubbles and Besemer teaches a different method by disclosing bubbles formed by the use of nitrogen. This statement alone does not effectively provide evidence why Besemer cannot be applied to the instant claims. Simply because the bubbles are formed differently doesn't mean that Besemer reference cannot be applied, especially since the claimed phrase that recites the bubble

removing process is broad enough to encompass scenarios other than what is disclosed in the specification. In addition, the claimed invention is not directed to how bubbles are formed, but rather that they are removed by a process. Since Besemer does teach a process of removing bubbles, Besemer anticipates claimed limitation. To further clarify this point, claim 2, lines 20-21, merely states the broad phrase "wherein bubble removing processing for removing bubbles, which are present in the liquid, from the liquid is performed during the flowing of the liquid". Therefore, since Besemer teaches inlet and outlets to allow for bubbles to be removed from circulation, the instant phrase is anticipated, and Applicant's arguments are not found convincing.

With regards to Applicant's third point above, Applicant specifically argues on page 3, last paragraph, that bubbles cannot be removed by merely causing fluid to flow in the vertical direction in the present invention and that it is require to provide a process for positively removing or dissolving bubbles in the present invention.

Applicant's arguments have been fully considered but are not persuasive. First of all, it is not clear how the argument of positively removing or dissolving bubbles supports the traversal that Besemer does not teach or suggest causing fluid to flow across the porous adsorptive regions. As stated above, Besemer clearly teaches a bubble removing process by disclosing that inlets and outlets placed at the highest and lowest positions in a cavity will remove bubbles, thereby teaching a "bubble removing process". Regarding the flow "across" the porous adsorptive regions, the specification does not disclose which direction is considered to be "across". The term, as one of ordinary skill in the art at the time of the invention would recognize, indicates a general

directional movement, and does not necessarily define movement through a porous region, as provided by one example in the specification. Since the specification does not define "across", and the instant claims recite the term broadly, flow "across" a region can be properly interpreted to indicate flow over a region. Therefore, since Besemer teaches that fluids are introduced by a fluid delivery system to a wafer containing immobilized probes, the fluid would necessarily flow across the wafer, thereby anticipating the claimed invention.

Therefore, since Applicant's arguments are not found to be convincing, the rejection under 35 U.S.C. 102(b) as applied in the previous Office Action is hereby maintained.

10. On pages 4-5 of the Remarks, Applicant traverses the rejection of claims 8-9 and 11-12 under 35 U.S.C. 103(a) as obvious over Besemer et al in view of Bronstein et al (US 5,543,295). Applicant argues that Bronstein et al does not remedy the alleged deficiencies of Besemer and that there is no motivation to combine the references. Specifically, Applicant contends that Besemer is related to a means for performing a bio-assay, whereas Bronstein is related to an improvement in chemiluminescent dioxetanes, and that even if the references were combined the step of performing a bubble removing process in claim 2 and the step of performing bubble dissolving process in claim 3 would not be taught.

Applicant's arguments have been fully considered but are not persuasive. As stated above, since Besemer teaches each and every limitation of parent claims 2-3,

there is therefore no deficiency in claim limitations that are not taught by Besemer. With regards to Applicant's arguments that there is no motivation to combine Besemer and Bronstein references, the previous Office Action and the rejection under 35 U.S.C. 103(a) supra indicate that dioxetane (i.e. labeling substance), as taught by Bronstein, is combined with Besemer, with the motivation of providing a water soluble reporter molecule for use in bioassays. One of ordinary skill in the art at the time of the invention would also have had reasonable expectation of success in including dioxetane with the method of Besemer since Besemer teaches that the ligand or receptor can be an enzyme, and dioxetane produces luminescence through enzymatic cleavage of a chromophore attached thereon.

Therefore, since there is no deficiency in the application of Besemer reference to the parent claims, and there is proper motivation for combining Besemer and Bronstein references, the rejection under 35 U.S.C. 103(a) applied in the previous Office Action is maintained.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/28/05